# NICOTINIC DRUG TREATMENT IN ALZHEIMER'S DISEASE: FROM THE LABORATORY TO THE CLINIC

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Dysfunction in cholinergic neurons plays some role in the cognitive and perhaps noncognitive or behavioral impairments seen in Alzheimer's disease and related dementias. First generation therapies have focused on cholinesterase inhibition. Tacrine or Cognex is now available in the United States and France. Second generation cholinergic therapeutics have focused on selective muscarinic cholinergic receptor agonists. Xanomeline (Lilly) CI979 (Warner-Lambert Parke- Davis) and SB202026 (Smithkline Beecham) are examples. Although alterations in M2 subtypes of muscarinic receptors and receptor decoupling have been claimed in Alzheimer's disease, the major cholinergic neurotransmittor receptor alteration is the loss of nicotinic receptors. A number of epidemiological studies have also shown that in Alzheimer's disease and Parkinson's disease smoking provides a "protective" effect. The biological basis for this epidemiological observation may relate to the fact that smoking increases nicotinic receptors in brain. The development of nicotinic receptor agonists may represent exciting diagnostic and therapeutic options. Nicotinic receptors can be imaged using positron emission tomography and has been used in Sweden to track therapeutic interventions. Nicotine itself has been administered to patients with Alzheimer's disease and normal older controls with mixed results. ABT418 (Abbott) has shown good preclinical and promising initial clinical results for the treatment of Alzheimer's disease. This compound binds to a specific subpopulation as nicotinic receptors found in human and animal brain. Ultimately, the treatment of Alzheimer's disease will require compounds that provide symptomatic benefits for both cognitive and noncognitive symptoms as well as others that preserve neuronal viability and thus slow the progression of the disease.

Source: https://www.industrydocuments.ucsf.edu/docs/krdb0000